Online Supplement

Supplemental Methods

Blood sampling and laboratory methods

Blood samples for determination of hs-cTnT and I were collected into tubes containing potassium EDTA or serum at presentation to the ED and serially thereafter. Serial sampling was discontinued when a patient was discharged or transferred to the catheter laboratory for treatment. After centrifugation, samples were either analysed directly or frozen at -80°C until they were assayed in a blinded fashion in a dedicated core laboratory.

According to the manufacturer, the hs-cTnT assay (Elecsys 2010 high-sensitivity troponin T, Roche Diagnostics, Rotkreuz, Switzerland) has a 99th percentile concentration of 14 ng/L with a corresponding coefficient of variation (CV) of 10% at 13 ng/L.[22] Limit of blank (LoB) and limit of detection (LoD) have been determined to be 3 ng/L and 5 ng/L. None of the hs-cTnT measurements in this analysis were affected by the 2010-2012 calibration shift.[23]

The hs-cTnI assay (ARCHITECT High Sensitive STAT Troponin I, Abbott Laboratories, IL, USA) has a 99th percentile concentration of 26.2 ng/L with a corresponding CV of <5% and a limit of detection (LoD) of 1.9 ng/L.[24]

ESC hs-cTnT/I-0/1h-algorithms

The ESC hs-cTnT/I-0/1h-algorithms were optimized for the early rule-out and rule-in of AMI and incorporate assay-specific hs-cTnT/I concentrations at ED presentation and their absolute changes within 1h.[4] Selection of these two parameters was based on the very high diagnostic accuracy for AMI achieved.[16][25] The algorithms

for hs-cTnT (Elecsys) and hs-cTnI (Architect) were derived and validated in recent studies.[10][16][19][26]

The rule-out criteria for hs-cTnT are defined as an undetectable (<5 ng/L) concentration at presentation or a baseline hs-cTnT concentration of less than 12 ng/L and an absolute change within the first 1 hour of less than 3 ng/L. Rule-in is defined by a baseline hs-cTnT concentration of at least 52 ng/L *or* an absolute change in hs-cTnT within the first 1 hour of at least 5 ng/L.

The rule-out criteria for hs-cTnI were defined as undetectable concentration (<2 ng/L) at presentation or a baseline hs-cTnI concentration of less than 5 ng/L and an absolute change within the first 1 hour of less than 2 ng/L. Rule-in is defined by a baseline hs-cTnI concentration of at least 52 ng/L *or* an absolute change in hs-cTnI within the first 1 hour of at least 6 ng/L. The remaining patients were triaged towards the observe zone (**Supplemental Figure 2A and 2B**).

Supplemental Results

Algorithms using hs-cTnI

A total of 2828 patients were eligible for the analysis using hs-cTnI (**Supplemental Figure 1B).** Patients triaged towards rule-out by the ESC hs-cTnI-0/1h-algorithm and its extended algorithm were younger, and less often had cardiovascular risk factors, preexisting CAD, ECG abnormalities, and cardiovascular medication**, Supplemental Table 5 and 6).**

Prognostic performance for MACE

MACE was adjudicated in 480 patients (17%, **Supplemental Table 7 and 8).** The ESC hs-cTnI-0/1h-algorithm triaged significantly more patients towards rule-out as

compared to the extended algorithm 52% (95%CI 49.9-53.6) versus 27% (95%CI 25.1-28.4), p<0.001).

Among patients triaged towards rule-out, MACE rate was 0.9% (95%CI 0.5-1.5%) for the ESC hs-cTnI-0/1h-algorithm and 0.1% (95%CI 0.0-0.6%) for the extended algorithm. This resulted in a sensitivity of 97.3% (95%CI 95.4-98.4) versus 99.8% (95%CI 98.8-100), NPV of 99.1% (95%CI 98.5-99.5) versus 99.9% (95%CI 99.3-100), p<0.01 and p=0.033, respectively; **Supplemental Figure 3A,3B and 3C. Supplemental Table 9**).

Among patients triaged towards rule-in, specificity and PPV for MACE were comparable using the ESC hs-cTnI-0/1h-algorithm and the extended algorithm (Specificity: 90.7% (95%CI 89.5-91.8) versus 88.3% (95%CI 87-89.5) p=0.301) and PPV: 63.3% (95%CI 59.3-67.1) versus 60.4% (95%CI 56.9-63.8) p=0.671) **(Supplemental Figure 3A,3B and 3C, Supplemental Table 9**).

Overall-efficacy (rule-out or rule-in) was also higher for the ESC hs-cTnI-0/1h-algorithm versus the extended algorithm (73% (95%CI 71.1-74.4) versus 49% (95%CI 47.2-50.9), p<0.001; **Supplemental Figure 3A and 3B**).

Prognostic performance for MACE+UA

Among patients triaged towards rule-out, MACE+UA rate was 6.8% (95%CI 5.5-8.2) for the ESC hs-cTnI-0/1h-algorithm and 1.5% (95%CI 0.7-2.6) for the extended algorithm (**Supplemental Figure 3A, 3B and 3C and Supplemental Table 7 and 8**). Among patients triaged towards rule-out, the ESC hs-cTnI-0/1h-algorithm had higher sensitivity, NPV and negative LR as compared to the extended algorithm: 86.5% (95%CI 83.9-88.8) versus 98.5 (95%CI 97.3-99.2); p<0.001; 93.2 (95%CI 91.8-94.4)

versus 98.5 (95%CI 97.4-99.2); p<0.001; and 0.21 (95%CI 0.17-0.25) versus 0.04 (95%CI 0.02-0.08), respectively (**Supplemental Table 9).**

Subgroup analyses using the hs-cTnI assay resulted in similar findings as compared to the hs-cTnT assay (**Supplemental Table 12**).

Supplemental Table 1 **STARD checklist for reporting studies of diagnostic accuracy**

Section & Topic	No	Item	Reported on page #
TITLE OR ABSTRACT			
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)	2
ABSTRACT			
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)	2-3
INTRODUCTION			
	3	Scientific and clinical background, including the intended use and clinical role of the index test	4-5
	4	Study objectives and hypotheses	4-5
METHODS			
Study design	**5**	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)	6
Participants	**6**	Eligibility criteria	6
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)	6
	8	Where and when potentially eligible participants were identified (setting, location and dates)	6
	9	Whether participants formed a consecutive, random or convenience series	6
Test methods	**10a**	Index test, in sufficient detail to allow replication	6-7
	10b	Reference standard, in sufficient detail to allow replication	7-8
	11	Rationale for choosing the reference standard (if alternatives exist)	7-8
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory	7-9
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory	7-9

	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test	7-9
	13b	Whether clinical information and index test results were available to the assessors of the reference standard	7-9
Analysis	**14**	Methods for estimating or comparing measures of diagnostic accuracy	7-10
	15	How indeterminate index test or reference standard results were handled	7-10
	16	How missing data on the index test and reference standard were handled	7-10
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory	7-10
	18	Intended sample size and how it was determined	n/a
RESULTS			
Participants	**19**	Flow of participants, using a diagram	Supplemental Figure 1
	20	Baseline demographic and clinical characteristics of participants	Supplemental Tables 2-5
	21a	Distribution of severity of disease in those with the target condition	11-13
	21b	Distribution of alternative diagnoses in those without the target condition	11-13
	22	Time interval and any clinical interventions between index test and reference standard	11-13
Test results	**23**	Cross tabulation of the index test results (or their distribution) by the results of the reference standard	11-13
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)	11-13
	25	Any adverse events from performing the index test or the reference standard	Table 3
DISCUSSION			
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability	17
	27	Implications for practice, including the intended use and clinical role of the index test	16-18
OTHER INFORMATION			
	28	Registration number and name of registry	6
	29	Where the full study protocol can be accessed	6
	30	Sources of funding and other support; role of funders	20-21

Supplemental Table 2 Baseline Characteristics ESC hs-cTn-0/1h-algorithm using hs-cTnT

	all patients		Rule-Out		Observe Zone		Rule-In	
	(n = 3123)		(n = 1880; 60%)		(n = 738; 24%)		(n = 505; 16%)	
Age, years, median (IQR)	61	(49 - 74)	54	(44 - 64)	74	(65 - 81)	72	(59 - 80)
Male, sex, n (%)	2116	68%	1226	65%	544	74%	346	69%
BMI, kg/m², median (IQR)	27	(24 - 30)	26	(24 - 30)	27	(24 - 30)	26	(24 - 29)
Risk factors, n (%)								
Hypertension	1911	61%	914	49%	629	85%	368	73%
Hypercholesterolemia	1538	49%	746	40%	501	68%	291	58%
Diabetes	550	18%	232	12%	199	27%	119	24%
Current smoking	782	25%	558	30%	113	15%	111	22%
History of smoking	1172	38%	621	33%	335	45%	216	43%
History, n (%)								
Coronary artery disease	1038	33%	442	24%	404	55%	192	38%
Previous myocardial infarction	742	24%	302	16%	290	39%	150	30%
Previous revascularization	858	28%	380	20%	332	45%	146	29%
Peripheral artery disease	162	5.2%	43	2.3%	70	9.5%	49	9.7%
Previous stroke	174	5.6%	61	3.2%	64	8.7%	49	9.7%
Positive family history	469	15%	318	17%	78	11.0%	73	15%
Chest pain onset ≤3h	1179	38%	745	40%	241	33%	193	38%
Chest pain onset >3h	1944	62%	1135	60%	497	67%	312	62%
ECG findings, n (%)								
Left bundle branch block	117	3.7%	24	1.3%	56	7.6%	37	7.3%
ST-segment elevation	53	1.7%	38	2.0%	9	1.2%	6	1.2%
ST-segment depression	323	10%	72	3.8%	105	14%	146	29%
T-wave inversion	343	11%	103	5.5%	129	18%	111	22%
No significant ECG abnormalities	2276	74%	1545	82%	473	64%	258	51%

Medication at entry n (%)								
Aspirin/Thienopyridin	1211	39%	543	29%	440	60%	228	45%
B-blockers	1078	35%	484	26%	403	55%	191	38%
ACE/AT2- Inhibitors	1230	39%	536	29%	458	62%	236	47%
Calcium- Antagonists	467	15%	195	10%	180	24%	92	18%
Nitrates	337	11%	109	5.8%	152	21%	76	15%
Statins	1110	36%	508	27%	410	56%	192	38%
in hospital procedures n (%)								
Coronary angiography	715	23%	177	9.4%	207	28%	331	66%
Percutaneous coronary intervention	402	13%	73	3.9%	118	16%	211	42%
CABG	60	1.9%	7	0.4%	19	2.6%	34	6.7%
Ergometry	744	24%	470	25%	192	26%	82	16%
Myocardial perfusion scanning	324	10%	169	9.0%	122	17%	33	6.5%

Table Legend: BMI: body mass index; BNP: brain natiruretic peptide; ECG: electrocardiography.

ACE: angiotensin converting enzyme; AT1: angiotensin 1; CABG: coronary artery bypass graft; IQR: interquatile ranges.

Supplemental Table 3 Baseline Characteristics Extended Algorithm using hs-cTnT

	all patients		Rule-Out		Observe Zone		Rule-In	
	(n = 3123)		(n = 1393; 45%)		(n = 928; 30%)		(n = 802; 26%)	
Age, years, median (IQR)	61	(49 - 74)	53	(43 - 63)	66	(54 - 76)	74	(61 - 81)
Male, sex, n (%)	2116	68%	898	65%	653	70%	565	70%
BMI, kg/m², median (IQR)	27	(24 - 30)	26	(24 - 30)	27	(24 - 30)	26	(24 - 29)
Risk factors, n (%)								
Hypertension	1911	61%	609	44%	673	73%	629	78%
Hypercholesterolemia	1538	49%	469	34%	559	60%	510	64%
Diabetes	550	18%	145	10.0%	198	21%	207	26%
Current smoking	782	25%	431	31%	198	21%	153	19%
History of smoking	1172	38%	440	32%	372	40%	360	45%
History, n (%)								
Coronary artery disease	1038	33%	238	17%	422	46%	378	47%
Previous myocardial infarction	742	24%	159	11%	302	33%	281	35%
Previous revascularization	858	28%	205	15%	351	38%	302	38%
Peripheral artery disease	162	5.2%	27	1.9%	51	5.5%	84	11%
Previous stroke	174	5.6%	45	3.2%	54	5.8%	75	9.4%
Positive family history	469	15%	231	17%	131	14%	107	13%
Chest pain onset <3h	1179	38%	565	41%	328	35%	286	36%
Chest pain onset <3h	1944	62%	828	59%	600	65%	516	64%
ECG findings, n (%)								
Left bundle branch block	117	3.7%	14	1.0%	51	5.5%	52	6.5%
ST-segment elevation	53	1.7%	0	0%	40	4.3%	13	1.6%
ST-segment depression	323	10%	0	0%	93	10%	230	29%
T-wave inversion	343	11%	0	0%	134	14%	209	26%
No significant ECG abnormalities	2276	74%	1393	100%	526	57%	357	45%
Medication at entry n (%)								

Aspirin/Thienopyridin	1211	39%	311	22%	467	50%	433	54%
B-blockers	1078	35%	296	21%	413	45%	369	46%
ACE/AT2- Inhibitors	1230	39%	331	24%	477	51%	422	53%
Calcium- Antagonists	467	15%	126	9%	159	17%	182	23%
Nitrates	337	11%	59	4.2%	120	13%	158	20%
Statins	1110	36%	293	21%	442	48%	375	47%
in hospital procedures n (%)								
Coronary angiography	715	23%	70	5.0%	190	21%	455	57%
Percutaneous coronary intervention	402	13%	23	1.7%	97	11.0%	282	35%
CABG	60	1.9%	3	0.2%	13	1.4%	44	5.5%
Ergometry	744	24%	303	22%	287	31%	154	19%
Myocardial perfusion scanning	324	10%	97	7.0%	145	16%	82	10%

Table Legend: BMI: body mass index; BNP: brain natiruretic peptide; ECG: electrocardiography.

ACE: angiotensin converting enzyme; AT1: angiotensin 1; CABG: coronary artery bypass graft; IQR: interquatile ranges.

Supplemental Table 4 False Ruled-Out patients

Age	Sex	Time from CPO to first study blood draw, h	Likelihood for ACS in %	History of CAD	hs-cTnT ad admission (ng/L)	hs-cTnT after 1h (ng/L)	ST-depression	T-inversion	MACE	Adjudicated Final Diagnosis
82#	male	12	20	yes	11	11	no	no	AV Block	arrhythmic disorder
47	female	2	40	no	8	11	yes	no	-	NSTEMI
62	male	1	60	yes	10	10	no	no	cardiac death	aortic dissection
53	male	12	90	yes	7	10	no	yes	NSTEMI 28 days later	UA
73	female	4	50	no	10	10	no	yes	AV Block	pneumonia
74	female	1	40	no	10	12	yes	no	-	NSTEMI
73	female	4	30	no	10	10	no	no	AV Block	arrhythmic disorder
63	female	3	70	no	8	10	no	no	NSTEMI 8 days later	arrhythmic disorder
67	female	1	30	no	6	7	no	no	-	NSTEMI
86	female	4	80	yes	8	7	no	no	-	NSTEMI
62	female	6	90	no	5	5	no	yes	NSTEMI 2 days later	UA

72#	female	8	0	no	9	9	no	no	cardiac arrest	neoplasia

Table legend: * for MACE; # also missed patients by extended algorithm;

CPO: chest pain onset; ACS: acute coronary syndrome; CAD: coronary artery disease; hs-cTnT: high sensitivity cardiac troponin T;

MACE: major adverse cardiac events; AV-Block: atrioventricular block;

NSTEMI: non ST-segment elevation myocardial infarction (all Type 1 Myocardial Infarction); UA: unstable angina

Supplemental Table 5 Baseline Characteristics ESC hs-cTn 0/1h-algorithm using hs-cTnI

	All patients (n = 2828)		Rule-Out (n = 1464; 52%)		Observe Zone (n = 770; 27%)		Rule-In (n = 594; 21%)	
Age, years, median (IQR)	62	49-74	53	43-64	72	60-80	70	57-79
Male, sex, n (%)	1928	68%	959	66%	553	72%	416	70%
BMI, kg/m², median (IQR)	27	24-30	26	24-29	27	25-30%	27	24-29
Risk factors, n (%)								
Hypertension	1731	61%	675	46%	625	81%	431	73%
Hypercholesterolemia	1390	49%	550	37%	498	65%	342	58%
Diabetes	507	18%	180	12%	184	24%	143	24%
Current smoking	709	25%	441	30%	127	17%	141	24%
History of smoking	1070	38%	473	32%	345	45%	252	42%
History, n (%)								
Coronary artery disease	941	33%	309	21%	392	51%	240	40%
Previous myocardial infarction	665	24%	197	14%	289	38%	179	30%
Previous revascularization	770	27%	266	18%	317	41%	187	32%
Peripheral artery disease	147	5.2%	26	1.8%	64	8.3%	57	9.6%
Previous stroke	161	5.7%	50	3.4%	60	7.8%	51	8.6%
Positive family history	420	15%	239	16%	89	12.0%	92	16%
Chest pain onset ≤3h	1050	37%	586	40%	257	33%	207	35%
Chest pain onset >3h	1778	63%	878	60%	513	67%	387	65%
ECG findings, n (%)								
Left bundle branch block	109	3.9%	17	1.2%	58	7.5%	34	5.7%
ST-segment elevation	48	1.7%	26	1.8%	8	1.0%	14	2.4%
ST-segment depression	291	10%	48	3.3%	94	12%	149	25%
T-wave inversion	312	11%	72	4.9%	118	15%	122	21%
No significant ECG abnormalities	2111	75%	1265	86%	516	67%	330	56%
Medication at entry n (%)								

Aspirin/Thienopyridin	1091	39%	383	26%	425	55%	283	48%
B-blockers	955	34%	333	23%	385	50%	237	40%
ACE/AT2-Inhibitors	1099	39%	373	26%	440	57%	286	48%
Calcium-Antagonists	422	15%	135	9.2%	178	23%	109	18%
Nitrates	306	11%	76	5.2%	138	18%	92	16%
Statins	989	35%	367	25%	394	51%	228	38%
in hospital procedures n (%)								
Coronary angiography	656	23%	126	8.6%	180	23%	350	59%
Percutaneous coronary intervention	371	13%	47	3.2%	95	12%	229	39%
CABG	55	1.9%	3	0.2%	19	2.5%	33	5.6%
Ergometry	679	24%	353	24%	206	27%	120	20%
Myocardial perfusion scanning	304	11%	123	8.4%	127	17%	54	9.1%

Table Legend: BMI: body mass index; BNP: brain natiruretic peptide; ECG: electrocardiography.

ACE: angiotensin converting enzyme; AT1: angiotensin 1; CABG: coronary artery bypass graft; IQR: interquatile ranges.

Supplemental Table 6 Baseline Characteristics Extended Algorithm using hs-cTnI

	all patients (n = 2828)		Rule-Out (n = 755; 27%)		Observe Zone (n = 1442; 51%)		Rule-In (n = 631; 22%)	
Age, years, median (IQR)	62	49-74	49	39-60	65	53-76	70	57-79
Male, sex, n (%)	1928	68%	477	25%	1010	70%	441	70%
BMI, kg/m², median (IQR)	27	24-30	26	23-29	27	24-30	27	24-29
Risk factors, n (%)								
Hypertension	1731	61%	267	35%	1000	69%	464	74%
Hypercholesterolemia	1390	49%	199	26%	829	58%	362	57%
Diabetes	507	18%	63	8.3%	291	20%	153	24%
Current smoking	709	25%	238	32%	324	23%	147	23%
History of smoking	1070	38%	234	31%	566	39%	270	43%
History, n (%)								
Coronary artery disease	941	33%	83	11%	593	41%	265	42%
Previous myocardial infarction	665	24%	51	6.8%	417	29%	197	31%
Previous revascularization	770	27%	74	10%	490	34%	206	33%
Peripheral artery disease	147	5.2%	9	1.2%	74	5.1%	64	10%
Previous stroke	161	5.7%	20	2.6%	87	6.0%	54	8.6%
Positive family history	420	15%	133	18%	187	13%	100	16%
Chest pain onset ≤3h	1050	37%	298	40%	536	37%	216	34%
Chest pain onset >3h	1778	63%	457	60%	906	63%	415	66%
ECG findings, n (%)								
Left bundle branch block	109	3.9%	6	1.0%	67	4.6%	36	5.7%
ST-segment elevation	48	1.7%	0	0%	32	2.2%	16	2.5%
ST-segment depression	291	10%	0	0%	128	8.9%	163	26%
T-wave inversion	312	11%	0	0%	173	12.0%	139	22%
No significant ECG abnormalities	2111	75%	755	99%	1019	71%	337	53%
Medication at entry n (%)								

Aspirin/Thienopyridin	1091	39%	105	14%	683	47%	303	48%
B-blockers	955	34%	116	15%	582	40%	257	41%
ACE/AT2-Inhibitors	1099	39%	129	17%	661	46%	309	49%
Calcium-Antagonists	422	15%	48	6.4%	254	18%	120	19%
Nitrates	306	11%	15	2.0%	187	13%	104	17%
Statins	989	35%	111	15%	632	44%	246	39%
in hospital procedures n (%)								
Coronary angiography	656	23%	22	2.9%	265	18%	369	59%
Percutaneous coronary intervention	371	13%	6	1.0%	122	8.5%	243	39%
CABG	55	1.9%	0	0%	19	1.3%	36	5.7%
Ergometry	679	24%	107	14%	449	31%	123	20%
Myocardial perfusion scanning	304	11%	26	3.4%	222	15%	56	8.9%

Table Legend: BMI: body mass index; BNP: brain natiruretic peptide; ECG: electrocardiography.

ACE: angiotensin converting enzyme; AT1: angiotensin 1; CABG: coronary artery bypass graft; IQR: interquatile ranges.

Supplemental Table 7 MACE ESC hs-cTnI 0/1h-algorithm using hs-cTnI

	all patients (n = 2828)		Rule-Out (n = 1464; 52%)		Observe Zone (n = 770; 27%)		Rule-In (n = 594; 21%)	
MACE	480	17%	13	0.9%	91	12%	376	63%
MACE+UA	734	26%	99	6.8%	225	29%	410	69%
T1MI during index visit	393	14%	3	0.2%	57	7.4%	333	56%
T2MI during index visit	57	2.0%	4	0.3%	14	1.8%	39	6.6%
T1MI during follow up	33	1.2%	3	0.2%	13	1.7%	17	2.9%
UA	272	9.6%	89	6.1%	145	19%	38	6.4%
Cardiogenic shock	8	0.3%	0	0%	1	0.1%	7	1.2%
Ventricular arrhythmia	5	0.2%	0	0%	2	0.3%	3	0.5%
High-grade AV Block	9	0.3%	2	0.1%	2	0.3%	5	0.8%
Cardiac death	16	0.6%	0	0%	4	0.5%	12	2.0%
Non cardiac death	9	0.3%	1	0.1%	5	0.6%	3	0.5%

Table Legend: MACE: major adverse cardiac event, MACE-UA: major adverse cardiac event with unstable angina
T1MI: Type 1 myocardial infarction; T2MI: Type 2 myocardial infarction UA: unstable angina; values are presented in n and %

Supplemental Table 8 MACE Extended Algorithm using hs-cTnI

	all patients (n = 2828)		Rule-Out (n = 755; 27%)		Observe Zone (n = 1442; 51%)		Rule-In (n = 631; 23%)	
MACE	480	17%	1	0.1%	87	6.0%	392	62%
MACE+UA	734	26%	11	1.5%	290	20%	433	69%
T1MI during index visit	393	14%	0	0%	52	4.9%	366	56%
T2MI during index visit	57	2.0%	0	0.0%	13	1.2%	42	6.6%
T1MI during follow up	33	1.2%	0	0%	14	1.0%	19	3.0%
UA	272	9.6%	10	1.3%	189	18%	46	7.0%
Cardiogenic shock	8	0.3%	0	0%	0	0%	8	1.3%
Ventricular arrhythmia	5	0.2%	0	0%	2	0.1%	3	0.5%
High-grade AV Block	9	0.3%	0	0%	4	0.3%	5	0.8%
Cardiac death	16	0.6%	0	0%	3	0.2%	13	2.1%
Non cardiac death	9	0.3%	1	0.1%	3	0.2%	5	0.8%

Table Legend: MACE: major adverse cardiac event, MACE-UA: major adverse cardiac event with unstable angina

T1MI: Type 1 myocardial infarction; T2MI: Type 2 myocardial infarction UA: unstable angina; values are presented in n and %

Supplemental Table 9

hs-cTnI Algorithmic diagnostic perfomance for MACE

	ESC hs-cTnI-0/1h-algorithm % (95% CI)	Extended Algorithm % (95% CI)	
Rule-Out	n = 1464	n = 755	p-value
Sensitivity	97.3 (95.4-98.4)	99.4 (98.2-99.8)	p<0.001
NPV	99.1 (98.5-99.5)	99.7 (99.2-99.9)	p=0.004
Neg. LR	0.04 (0.03-0.08)	0.01(0.00-0.04)	
Rule-In	n = 594	n =631	
Specificity	90.7 (89.5-91.8)	89.7 (88.4-90.9)	p<0.001
PPV	63.3 (59.3-67.1)	61.9 (58.1-65.6)	p=0.011
Pos. LR	8.44 (7.37-9.66)	7.94 (7-9.02)	

hs-cTnI Algorithmic diagnostic perfomance for MACE+UA

	ESC hs-cTnI-0/1h-algorithm % (95% CI)	Extended Algorithm % (95% CI)	
Rule-Out	n = 1464	n = 755	p-value
Sensitivity	86.5 (83.9-88.8)	94.7(92.7-96)	p<0.001
NPV	93.2 (91.8-94.4)	96.5 (95.3-97.4)	p<0.001
Neg. LR	0.21 (0.17-0.25)	0.10 (0.08-0.14)	
Rule-In	n = 594	n = 631	
Specificity	91.2 (98.9-92.4)	90.4 (89.1-91.6)	p<0.001
PPV	69.0 (65.2-72.6)	68.3 (64.6-71.8)	p=0.194
Pos. LR	6.36 (5.46-7.40)	6.16 (5.33-7.12)	

Table Legend: MACE: major adverse cardiac event, MACE+UA: major adverse cardiac event with unstable angina

CI: confidence interval.NPV: negative predictive value, PPV: positive predictive value,

neg. LR: negative likelihood ratio, pos. LR: positive likelihood ratio

Supplemental Table 10

hs-cTnT Algorithmic diagnostic perfomance for MACE without T2MI

	ESC hs-cTnT-0/1h-algorithm % (95% CI)	Extended Algorithm % (95% CI)
Rule-Out	n = 1880	n = 1393
Sensitivity	97.4 (95.6 - 98.5)	98.9 (97.5 - 99.5)
NPV	99.4 (98.6 - 99.9)	99.6 (99.2 - 99.8)
Neg. LR	0.03 (0.02 - 0.07)	0.00 (0.00 - 0.03)
Rule-In	n = 505	n = 802
Specificity	94.2 (93.2 - 95)	85.9 (84.5 - 90.9)
PPV	69.5 (65.4 - 73.4)	53.2 (49.8 - 56.7)
Pos. LR	12.87 (10.94 - 15.13)	6.43 (5.83 - 7.09)

hs-cTnI Algorithmic diagnostic perfomance for MACE without T2MI

	ESC hs-cTnI-0/1h-algorithm % (95% CI)	Extended Algorithm % (95% CI)
Rule-Out	n = 1464	n = 755
Sensitivity	97.9 (96.1 - 98.9)	99.8 (98.7 - 100)
NPV	99.4 (98.8 - 99.7)	99.9 (99.5 - 100)
Neg. LR	0.03 (0.02 - 0.07)	0.00 (0.00 - 0.03)
Rule-In	n = 594	n = 631
Specificity	89.6 (88.4 - 90.8)	88.6 (87.3 - 89.8)
PPV	58.2 (54.2 - 62.1)	57 (53.1 - 60.8)
Pos. LR	7.68 (6.76 - 8.72)	7.29 (6.48 - 8.22)

Table Legend: MACE: major adverse cardiac event, MACE+UA: major adverse cardiac event with unstable angina

CI: confidence interval.NPV: negative predictive value, PPV: positive predictive value,

neg. LR: negative likelihood ratio, pos. LR: positive likelihood ratio

Supplemental Table 11 hs-cTnT **a**lgorithmic performance in Subgroup Analysis

Rule-out ESC hs-cTnT 0/1h-Algorithm for MACE

	Sensitivity (95%CI)	Specificity (95%CI)	NPV (95%CI)	PPV (95%CI)
females	0.939 (0.888 to 0.967)	0.752 (0.722 to 0.78)	0.986 (0.974 to 0.993)	0.393 (0.343 to 0.445)
males	0.992 (0.977 to 0.997)	0.703 (0.681 to 0.724)	0.998 (0.993 to 0.999)	0.420 (0.388 to 0.453)
≥ 62 years	0.974 (0.953 to 0.986)	0.511 (0.482 to 0.54)	0.984 (0.97 to 0.991)	0.398 (0.367 to 0.429)
< 62 years	0.985 (0.948 to 0.996)	0.890 (0.873 to 0.905)	0.998 (0.994 to 1)	0.460 (0.404 to 0.518)
CAD	0.984 (0.96 to 0.994)	0.557 (0.522 to 0.591)	0.991 (0.977 to 0.996)	0.414 (0.376 to 0.454)
non-CAD	0.971 (0.943 to 0.985)	0.790 (0.771 to 0.808)	0.994 (0.989 to 0.997)	0.411 (0.374 to 0.449)
cpo ≤ 2h	0.971 (0.928 to 0.989)	0.770 (0.737 to 0.8)	0.993 (0.981 to 0.997)	0.457 (0.401 to 0.515)
cpo > 2h	0.982 (0.963 to 0.991)	0.701 (0.68 to 0.722)	0.995 (0.989 to 0.997)	0.399 (0.369 to 0.431)
eGFR ≤ 60	0.986 (0.952 to 0.996)	0.273 (0.227 to 0.324)	0.978 (0.923 to 0.994)	0.380 (0.332 to 0.429)
eGFR > 60	0.973 (0.952 to 0.985)	0.784 (0.766 to 0.8)	0.994 (0.99 to 0.997)	0.427 (0.395 to 0.461)

Rule-out ESC hs-cTnT 0/1h-Algorithm for MACE+UA

	Sensitivity (95%CI)	Specificity (95%CI)	NPV (95%CI)	PPV (95%CI)
females	0.810 (0.749 to 0.859)	0.762 (0.732 to 0.79)	0.944 (0.923 to 0.959)	0.450 (0.399 to 0.502)
males	0.805 (0.772 to 0.835)	0.736 (0.713 to 0.757)	0.903 (0.885 to 0.918)	0.553 (0.52 to 0.585)
≥ 62 years	0.838 (0.806 to 0.865)	0.529 (0.498 to 0.561)	0.842 (0.811 to 0.869)	0.521 (0.489 to 0.553)
< 62 years	0.721 (0.657 to 0.777)	0.899 (0.882 to 0.914)	0.953 (0.94 to 0.963)	0.533 (0.475 to 0.589)
CAD	0.760 (0.719 to 0.796)	0.577 (0.536 to 0.617)	0.747 (0.704 to 0.785)	0.594 (0.554 to 0.633)
non-CAD	0.871 (0.831 to 0.902)	0.800 (0.781 to 0.818)	0.969 (0.959 to 0.977)	0.459 (0.421 to 0.498)
cpo ≤ 2h	0.826 (0.766 to 0.872)	0.792 (0.759 to 0.822)	0.937 (0.913 to 0.954)	0.549 (0.492 to 0.605)
cpo > 2h	0.801 (0.767 to 0.831)	0.728 (0.706 to 0.749)	0.909 (0.893 to 0.923)	0.518 (0.486 to 0.549)
eGFR ≤ 60	0.928 (0.884 to 0.956)	0.287 (0.236 to 0.344)	0.835 (0.746 to 0.897)	0.505 (0.455 to 0.555)

eGFR > 60	0.763 (0.727 to 0.795)	0.804 (0.786 to 0.82)	0.921 (0.907 to 0.933)	0.530 (0.497 to 0.564)
	Rule-out Extended Algorithm for MACE			
	Sensitivity (95%CI)	**Specificity (95%CI)**	**NPV (95%CI)**	**PPV (95%CI)**
females	0.993 (0.962 to 0.999)	0.395 (0.363 to 0.428)	0.997 (0.984 to 0.999)	0.219 (0.189 to 0.252)
males	0.997 (0.985 to 1)	0.330 (0.308 to 0.353)	0.998 (0.99 to 1)	0.244 (0.223 to 0.266)
≥ 62 years	0.995 (0.981 to 0.999)	0.178 (0.157 to 0.201)	0.990 (0.966 to 0.997)	0.286 (0.263 to 0.311)
< 62 years	1.000 (0.973 to 1)	0.494 (0.468 to 0.52)	1.000 (0.995 to 1)	0.158 (0.135 to 0.184)
CAD	0.996 (0.978 to 0.999)	0.144 (0.121 to 0.17)	0.991 (0.952 to 0.998)	0.271 (0.243 to 0.3)
non-CAD	0.996 (0.98 to 0.999)	0.442 (0.419 to 0.465)	0.999 (0.993 to 1)	0.212 (0.191 to 0.235)
cpo ≤ 2h	1.000 (0.973 to 1)	0.380 (0.345 to 0.417)	1.000 (0.986 to 1)	0.243 (0.21 to 0.28)
cpo > 2h	0.995 (0.981 to 0.999)	0.342 (0.321 to 0.364)	0.997 (0.989 to 0.999)	0.234 (0.214 to 0.255)
eGFR ≤ 60	0.986 (0.952 to 0.996)	0.089 (0.063 to 0.125)	0.935 (0.793 to 0.982)	0.328 (0.286 to 0.373)
eGFR > 60	1.000 (0.99 to 1)	0.390 (0.37 to 0.41)	1.000 (0.996 to 1)	0.214 (0.195 to 0.233)
	Rule-out Extended Algorithm for MACE+UA			
	Sensitivity (95%CI)	**Specificity (95%CI)**	**NPV (95%CI)**	**PPV (95%CI)**
females	0.969 (0.935 to 0.986)	0.413 (0.379 to 0.447)	0.982 (0.962 to 0.992)	0.284 (0.251 to 0.319)
males	0.977 (0.962 to 0.986)	0.373 (0.349 to 0.397)	0.976 (0.96 to 0.985)	0.387 (0.363 to 0.412)
≥ 62 years	0.976 (0.961 to 0.986)	0.203 (0.179 to 0.229)	0.933 (0.891 to 0.96)	0.428 (0.402 to 0.455)
< 62 years	0.972 (0.94 to 0.987)	0.519 (0.492 to 0.545)	0.992 (0.982 to 0.996)	0.243 (0.216 to 0.273)
CAD	0.970 (0.95 to 0.982)	0.175 (0.146 to 0.208)	0.877 (0.804 to 0.925)	0.489 (0.457 to 0.521)
non-CAD	0.982 (0.962 to 0.992)	0.456 (0.433 to 0.48)	0.993 (0.984 to 0.997)	0.260 (0.237 to 0.285)
cpo ≤ 2h	0.979 (0.948 to 0.992)	0.408 (0.37 to 0.447)	0.985 (0.962 to 0.994)	0.337 (0.299 to 0.377)
cpo > 2h	0.974 (0.958 to 0.984)	0.380 (0.357 to 0.403)	0.975 (0.96 to 0.985)	0.364 (0.341 to 0.388)
eGFR ≤	0.981 (0.952 to 0.992)	0.102 (0.071 to 0.144)	0.871 (0.711 to 0.949)	0.462 (0.416 to 0.508)

60 eGFR > 60	0.973 (0.957 to 0.983)	0.424 (0.403 to 0.445)	0.982 (0.971 to 0.989)	0.329 (0.308 to 0.352)

Table Legend: MACE: major adverse cardiac event,MACE+UA: major adverse cardiac event with unstable angina
CI: confidence interval, CAD: coronary artery disease, cpo: chest pain onset, eGFR: estimated glomerular filtration rate,
NPV: negative predictive value, PPV: positive predictive value

Supplemental Table 12 hs-cTnI algorithmic performance in Subgroup Analysis

Rule-out ESC hs-cTnI 0/1h-Algorithm for MACE

	Sensitivity (95%CI)	Specificity (95%CI)	NPV (95%CI)	PPV (95%CI)
females	0.956 (0.906 to 0.979)	0.652 (0.618 to 0.685)	0.988 (0.974 to 0.995)	0.327 (0.282 to 0.374)
males	0.980 (0.959 to 0.99)	0.603 (0.578 to 0.626)	0.993 (0.985 to 0.996)	0.350 (0.32 to 0.38)
≥ 62 years	0.966 (0.942 to 0.981)	0.421 (0.392 to 0.451)	0.974 (0.955 to 0.985)	0.359 (0.33 to 0.39)
< 62 years	0.992 (0.955 to 0.999)	0.782 (0.759 to 0.804)	0.999 (0.994 to 1)	0.303 (0.261 to 0.35)
CAD	0.970 (0.939 to 0.985)	0.427 (0.391 to 0.463)	0.977 (0.954 to 0.989)	0.358 (0.321 to 0.396)
non-CAD	0.976 (0.948 to 0.989)	0.702 (0.679 to 0.723)	0.995 (0.989 to 0.998)	0.330 (0.297 to 0.365)
cpo ≤ 2h	0.984 (0.944 to 0.996)	0.683 (0.646 to 0.719)	0.995 (0.983 to 0.999)	0.386 (0.334 to 0.44)
cpo > 2h	0.969 (0.945 to 0.982)	0.596 (0.572 to 0.619)	0.989 (0.981 to 0.994)	0.329 (0.301 to 0.359)
eGFR ≤ 60	0.978 (0.938 to 0.993)	0.266 (0.219 to 0.32)	0.963 (0.895 to 0.987)	0.389 (0.339 to 0.441)
eGFR > 60	0.971 (0.947 to 0.984)	0.668 (0.648 to 0.688)	0.993 (0.987 to 0.996)	0.327 (0.299 to 0.356)

Rule-out ESC hs-cTnI 0/1h-Algorithm for MACE+UA

	Sensitivity (95%CI)	Specificity (95%CI)	NPV (95%CI)	PPV (95%CI)
females	0.866 (0.808 to 0.908)	0.667 (0.632 to 0.701)	0.952 (0.93 to 0.968)	0.392 (0.346 to 0.441)
males	0.865 (0.834 to 0.891)	0.645 (0.62 to 0.67)	0.922 (0.903 to 0.937)	0.496 (0.465 to 0.528)
≥ 62 years	0.879 (0.849 to 0.903)	0.450 (0.417 to 0.483)	0.857 (0.822 to 0.886)	0.498 (0.466 to 0.529)
< 62 years	0.826 (0.766 to 0.874)	0.799 (0.775 to 0.82)	0.967 (0.954 to 0.977)	0.391 (0.344 to 0.439)
CAD	0.827 (0.788 to 0.86)	0.458 (0.415 to 0.501)	0.761 (0.71 to 0.805)	0.560 (0.521 to 0.598)
non-CAD	0.918 (0.882 to 0.944)	0.716 (0.693 to 0.738)	0.978 (0.968 to 0.985)	0.385 (0.35 to 0.421)
cpo ≤ 2h	0.893 (0.838 to 0.93)	0.716 (0.678 to 0.752)	0.955 (0.931 to 0.971)	0.495 (0.441 to 0.55)
cpo > 2h	0.855 (0.824 to 0.882)	0.630 (0.605 to 0.654)	0.922 (0.904 to 0.937)	0.458 (0.428 to 0.489)
eGFR ≤ 60	0.932 (0.886 to 0.96)	0.283 (0.229 to 0.343)	0.838 (0.742 to 0.903)	0.510 (0.458 to 0.562)

eGFR > 60	0.841 (0.808 to 0.869)	0.700 (0.679 to 0.72)	0.938 (0.924 to 0.949)	0.450 (0.42 to 0.481)
	Rule-out Extended Algorithm for MACE			
	Sensitivity (95%CI)	**Specificity (95%CI)**	**NPV (95%CI)**	**PPV (95%CI)**
females	0.993 (0.959 to 0.999)	0.362 (0.329 to 0.397)	0.996 (0.98 to 0.999)	0.215 (0.185 to 0.249)
males	1.000 (0.989 to 1)	0.302 (0.28 to 0.325)	1.000 (0.992 to 1)	0.238 (0.217 to 0.261)
≥ 62 years	0.997 (0.984 to 1)	0.149 (0.129 to 0.171)	0.994 (0.965 to 0.999)	0.282 (0.258 to 0.308)
< 62 years	1.000 (0.97 to 1)	0.465 (0.437 to 0.492)	1.000 (0.994 to 1)	0.152 (0.129 to 0.178)
CAD	1.000 (0.984 to 1)	0.117 (0.096 to 0.143)	1.000 (0.956 to 1)	0.272 (0.243 to 0.302)
non-CAD	0.996 (0.977 to 0.999)	0.410 (0.386 to 0.434)	0.999 (0.992 to 1)	0.203 (0.181 to 0.226)
cpo ≤ 2h	1.000 (0.97 to 1)	0.354 (0.317 to 0.392)	1.000 (0.983 to 1)	0.238 (0.204 to 0.276)
cpo > 2h	0.997 (0.984 to 0.999)	0.311 (0.289 to 0.333)	0.998 (0.989 to 1)	0.229 (0.209 to 0.251)
eGFR ≤ 60	0.993 (0.96 to 0.999)	0.080 (0.054 to 0.117)	0.958 (0.798 to 0.993)	0.340 (0.295 to 0.388)
eGFR > 60	1.000 (0.989 to 1)	0.356 (0.336 to 0.377)	1.000 (0.995 to 1)	0.205 (0.186 to 0.225)
	Rule-out Extended Algorithm for MACE+UA			
	Sensitivity (95%CI)	**Specificity (95%CI)**	**NPV (95%CI)**	**PPV (95%CI)**
females	0.983 (0.952 to 0.994)	0.381 (0.347 to 0.417)	0.989 (0.969 to 0.996)	0.283 (0.249 to 0.32)
males	0.986 (0.972 to 0.993)	0.342 (0.318 to 0.368)	0.983 (0.967 to 0.991)	0.377 (0.353 to 0.402)
≥ 62 years	0.985 (0.971 to 0.993)	0.172 (0.149 to 0.199)	0.950 (0.904 to 0.974)	0.425 (0.398 to 0.453)
< 62 years	0.984 (0.955 to 0.995)	0.488 (0.46 to 0.516)	0.995 (0.985 to 0.998)	0.231 (0.203 to 0.261)
CAD	0.984 (0.967 to 0.992)	0.148 (0.12 to 0.182)	0.916 (0.836 to 0.959)	0.491 (0.457 to 0.524)
non-CAD	0.987 (0.967 to 0.995)	0.423 (0.399 to 0.448)	0.994 (0.985 to 0.998)	0.249 (0.225 to 0.274)
cpo ≤ 2h	0.983 (0.951 to 0.994)	0.381 (0.342 to 0.422)	0.986 (0.961 to 0.995)	0.331 (0.293 to 0.373)
cpo > 2h	0.986 (0.972 to 0.993)	0.348 (0.324 to 0.372)	0.985 (0.971 to 0.992)	0.356 (0.333 to 0.381)
eGFR ≤	0.989 (0.962 to 0.997)	0.093 (0.062 to 0.137)	0.917 (0.742 to 0.977)	0.467 (0.418 to 0.515)

60 eGFR > 60	0.983 (0.969 to 0.991)	0.390 (0.368 to 0.412)	0.988 (0.977 to 0.994)	0.320 (0.298 to 0.343)

Table Legend: MACE: major adverse cardiac event,MACE+UA: major adverse cardiac event with unstable angina
CI: confidence interval, CAD: coronary artery disease, cpo: chest pain onset, eGFR: estimated glomerular filtration rate,
NPV: negative predictive value, PPV: positive predictive value

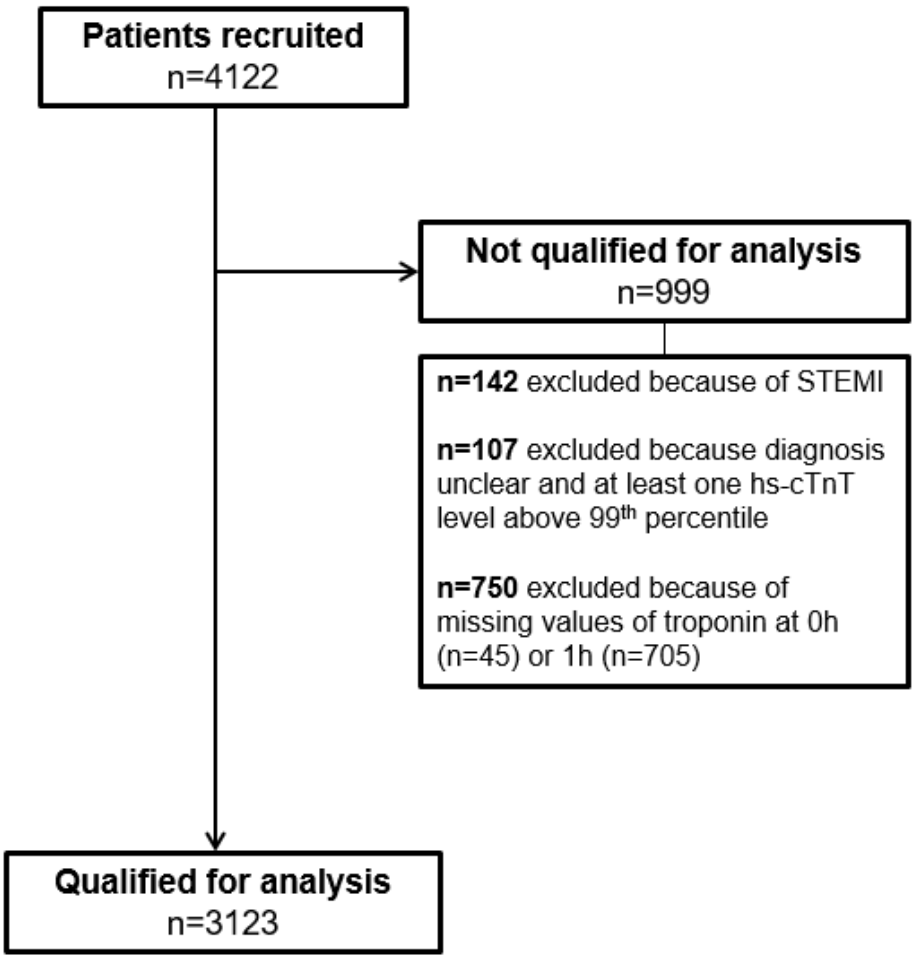


Figure 1A **Patient flow chart for hs-cTnT**

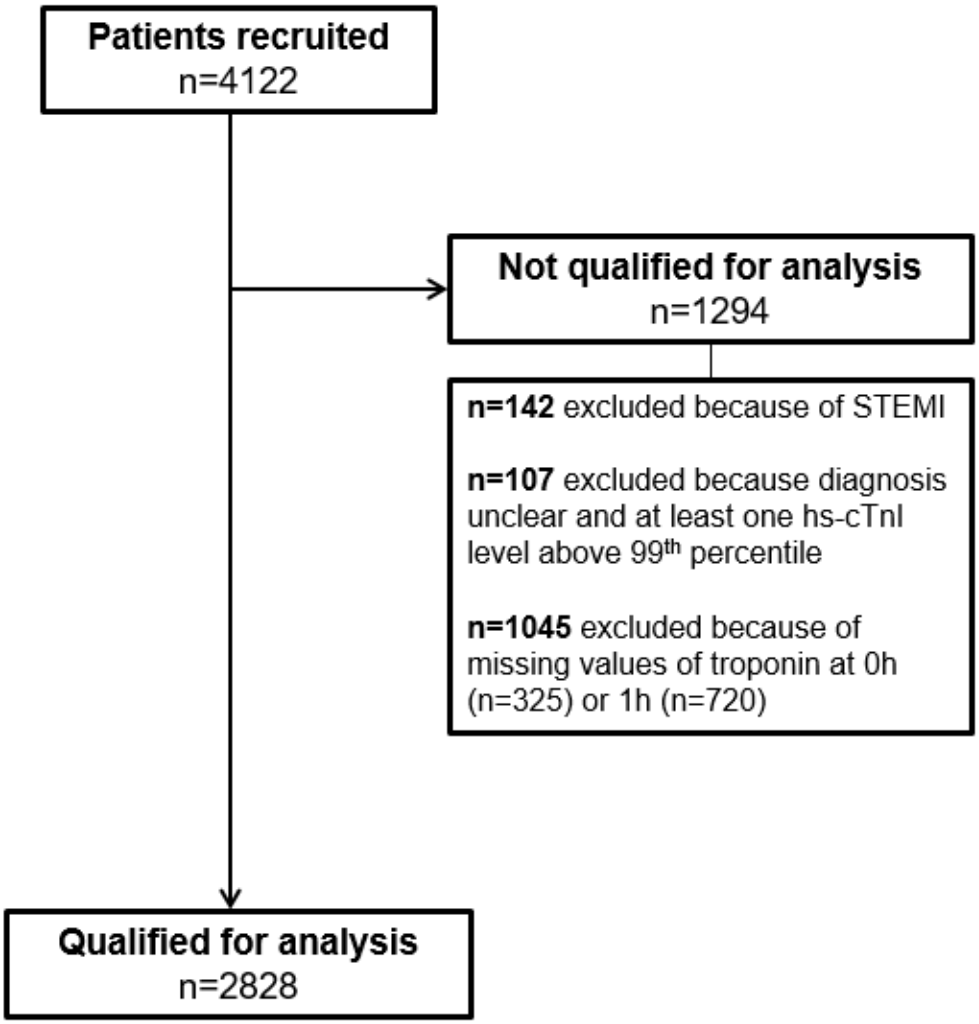
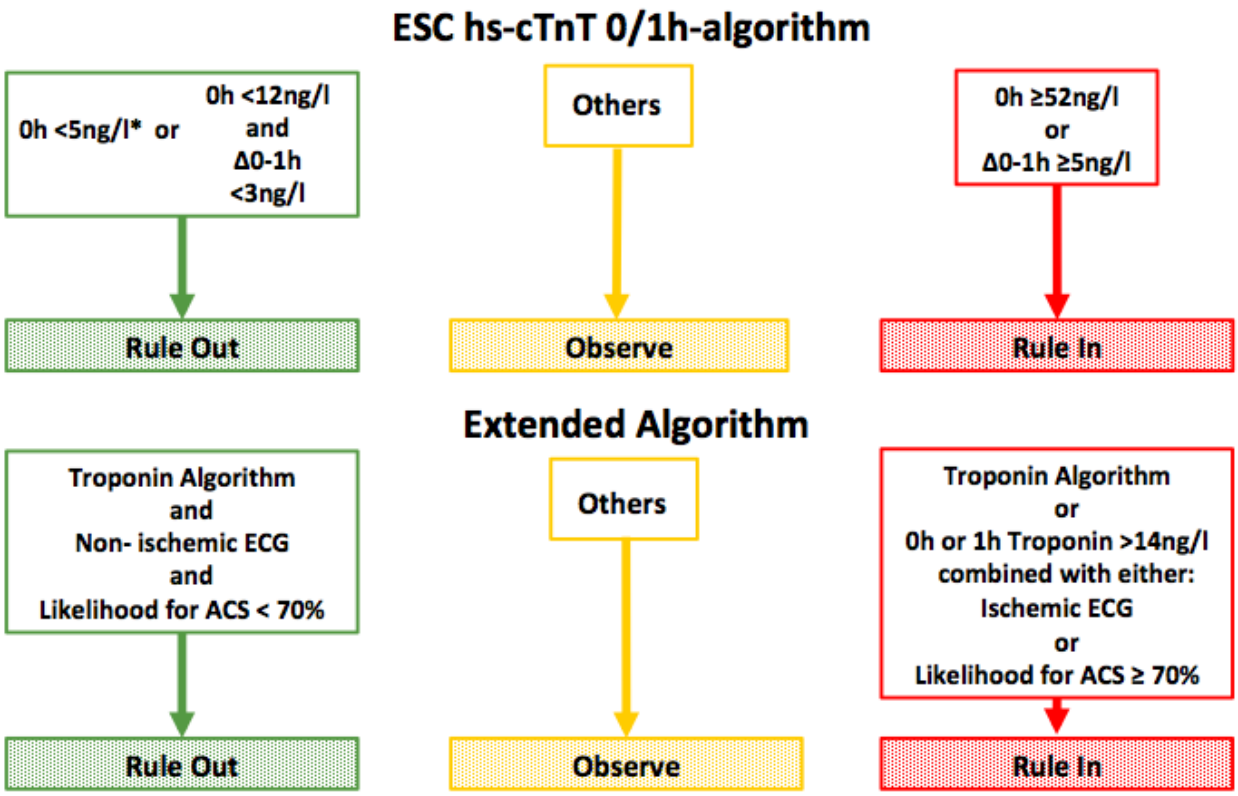
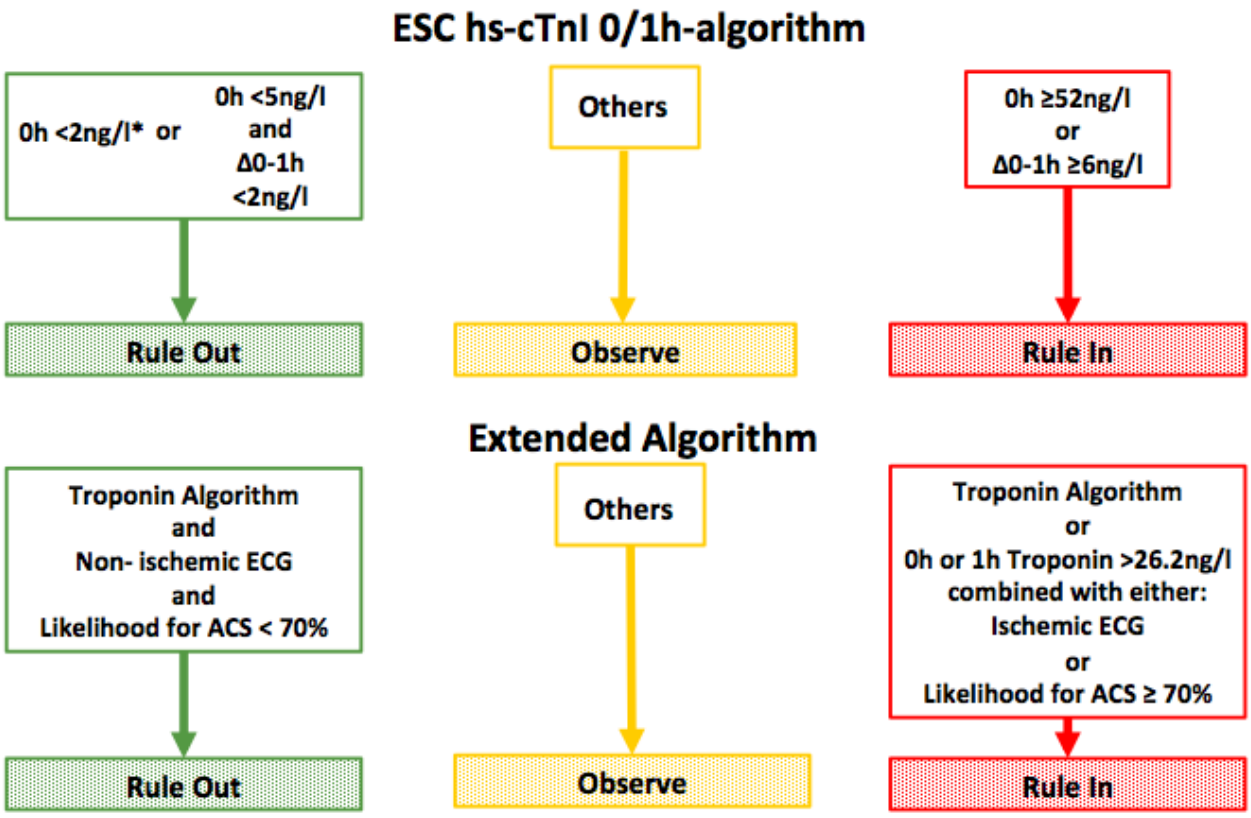


Figure 1B **Patient flow chart for hs-cTnI**



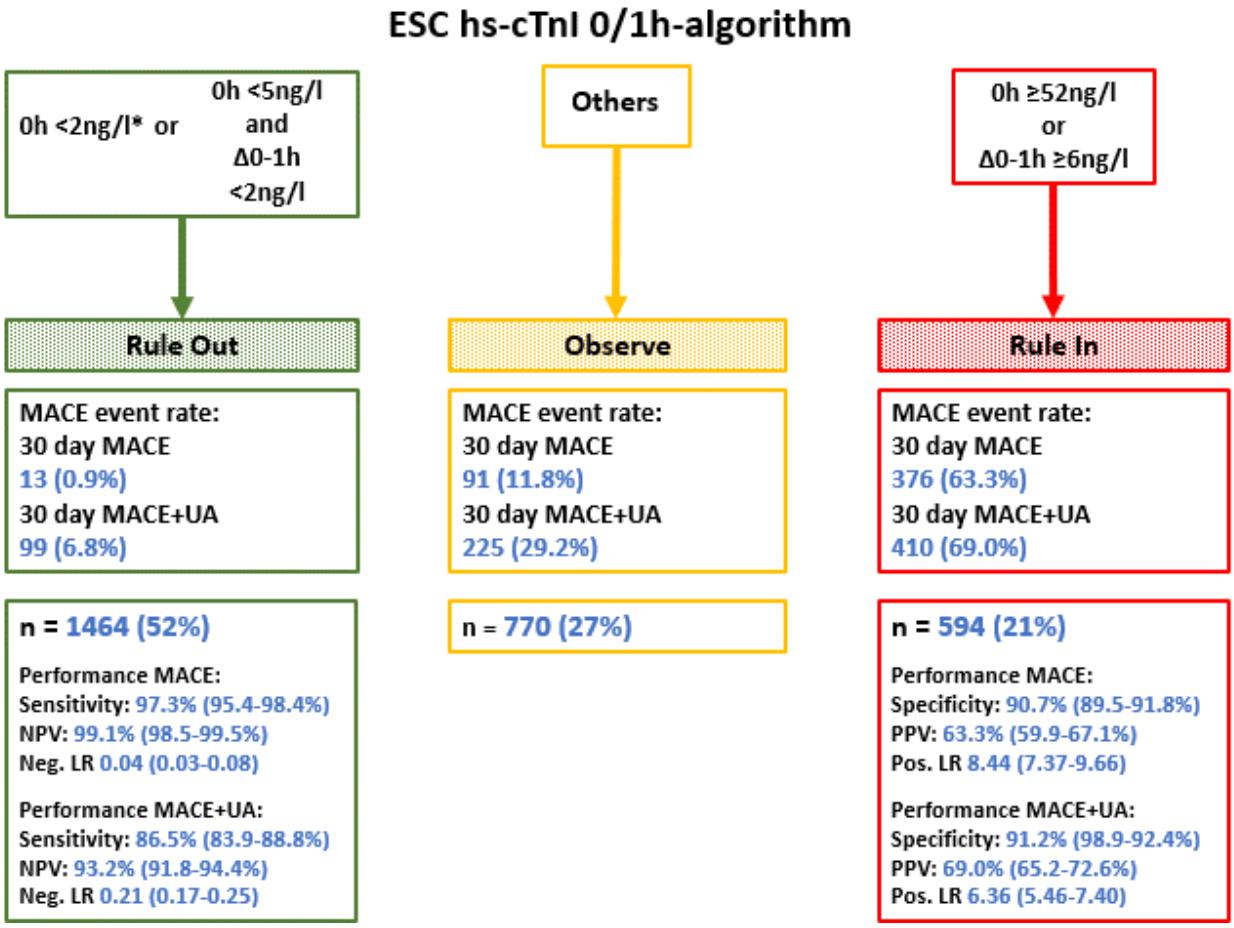
Supplemental Figure 2A **Criteria for ESC hs-cTnT 0/1h-algorithm and Extended algorithm using hs-cTnT**

Troponin algorithm classifying patients into rule-out, observe and rule-in. hs-cTn values are presented in ng/L. 0h/1h = hs-cTnT at presentation and after 1 hour. Δ0h-1h = absolute change of hs-cTnT within the first hour. MACE: major adverse cardiac event; MACE+UA: major adverse cardiac event with unstable angina; *if chest pain onset >3h



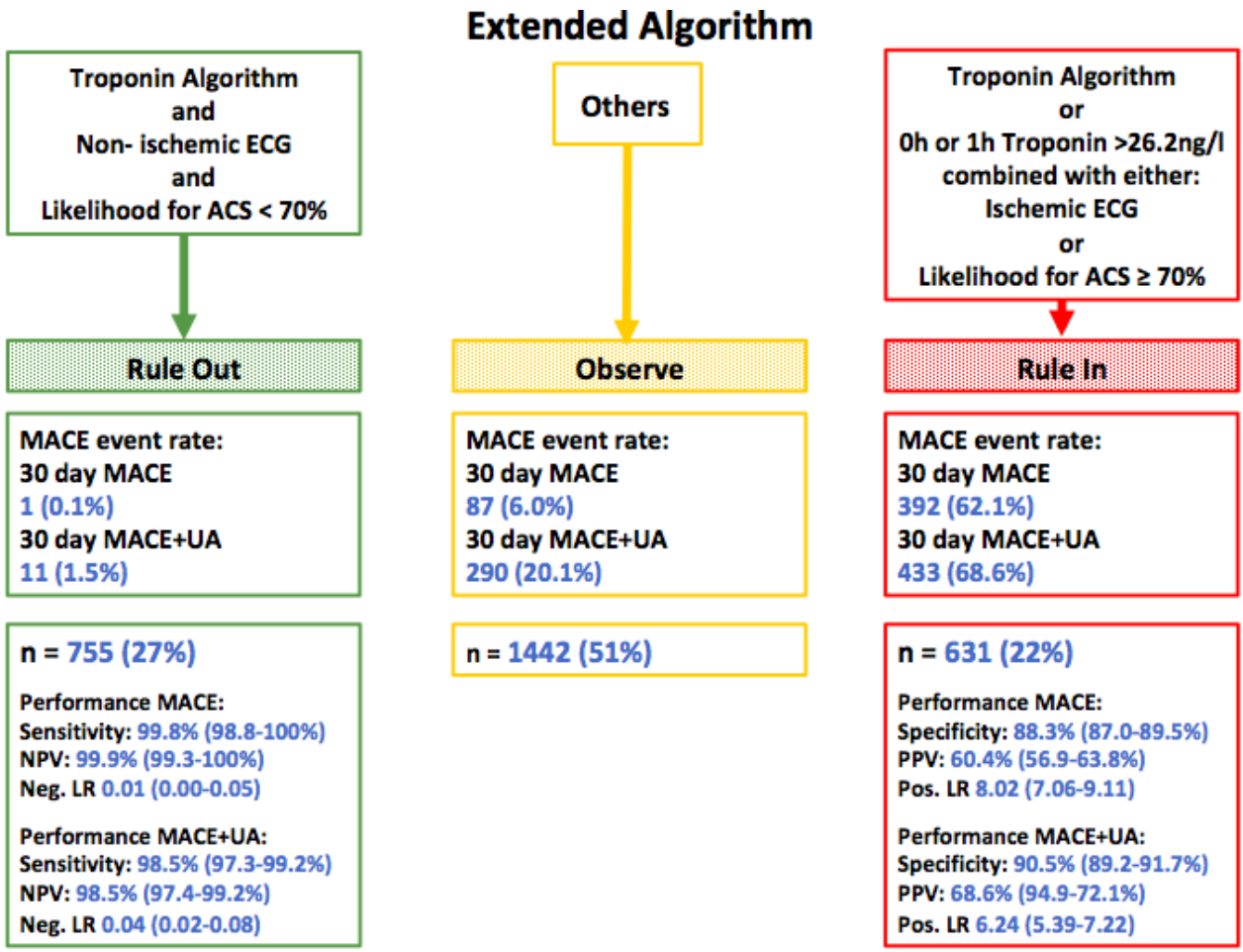
Supplemental Figure 2B **Criteria for ESC hs-cTnI 0/1h-algorithm and Extended algorithm using hs-cTnI**

Troponin algorithm classifying patients into rule-out, observe and rule-in. hs-cTn values are presented in ng/L. 0h/1h = hs-cTnI at presentation and after 1 hour. Δ0h-1h = absolute change of hs-cTnI within the first hour. MACE: major adverse cardiac event; MACE+UA: major adverse cardiac event with unstable angina; *if chest pain onset >3h



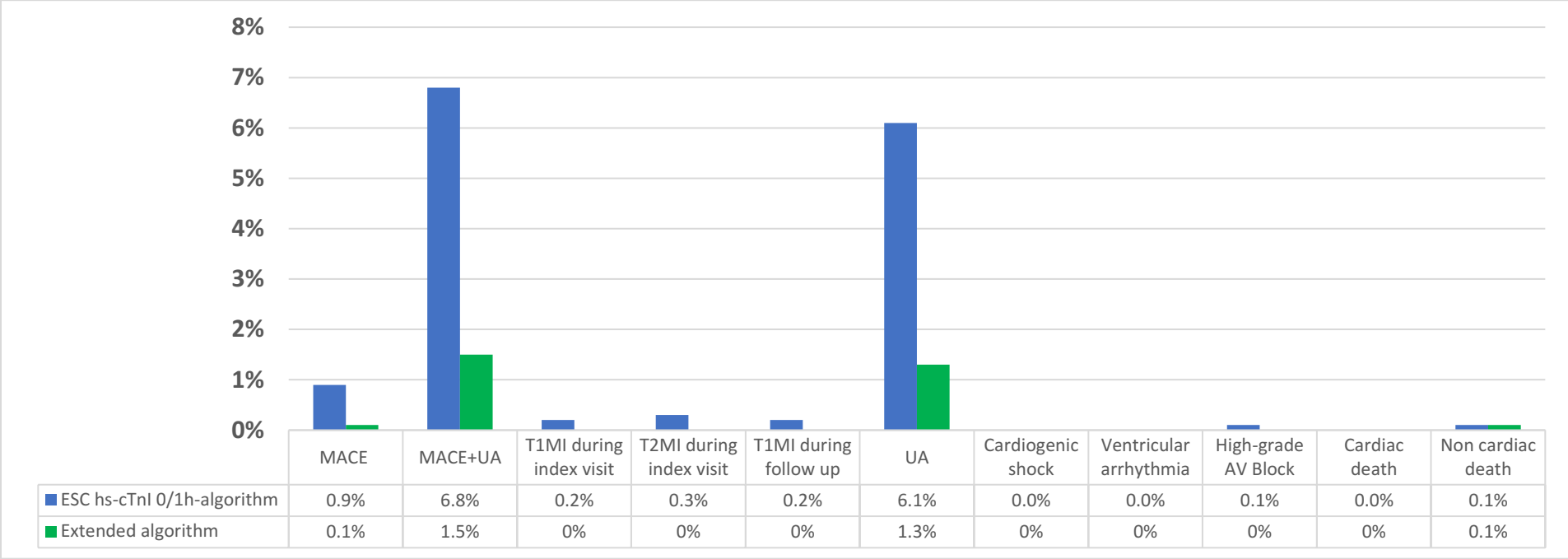
Supplemental Figure 3A **ESC hs-cTnI 0/1h-algorithm: criteria and performance for hs-cTnI**

ESC hs-cTnI-0/1h-algorithm classifying patients into rule-out, observe and rule-in. hs-cTn values are presented in ng/L. 0h/1h = hs-cTnI at presentation and after 1 hour. Δ0h-1h = absolute change of hs-cTnI within the first hour. MACE: major adverse cardiac event; MACE+UA: major adverse cardiac event with unstable angina; NPV: negative predictive value; PPV: positive predictive value, Pos.LR: positive likelihood ratio; Neg.LR: negative likelihood ratio; *if chest pain onset >3h



Supplemental Figure 3B **Extended algorithm: criteria and performance for hs-cTnI**

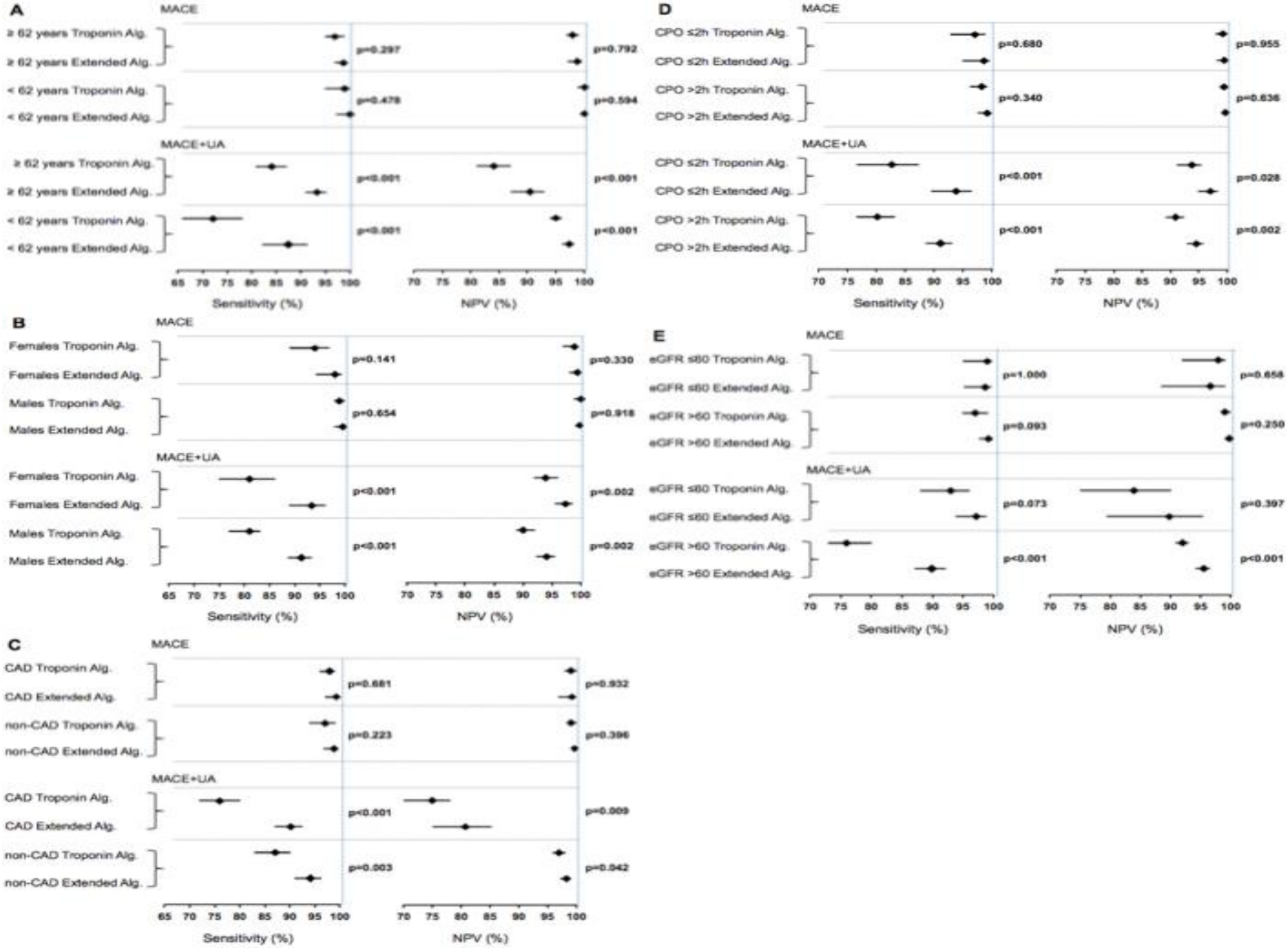
Troponin algorithm combined with ECG criteria and likelihood for acute coronary syndrome (ACS) classifying patients into rule-out, observe and rule-in. MACE: major adverse cardiac event; MACE+UA: major adverse cardiac event with unstable angina; NPV: negative predictive value; PPV: positive predictive value, Pos.LR: positive likelihood ratio; Neg.LR: negative likelihood ratio; *if chest pain onset >3h



	MACE	MACE+UA	T1MI during index visit	T2MI during index visit	T1MI during follow up	UA	Cardiogenic shock	Ventricular arrhythmia	High-grade AV Block	Cardiac death	Non cardiac death
ESC hs-cTnI 0/1h-algorithm	0.9%	6.8%	0.2%	0.3%	0.2%	6.1%	0.0%	0.0%	0.1%	0.0%	0.1%
Extended algorithm	0.1%	1.5%	0%	0%	0%	1.3%	0%	0%	0%	0%	0.1%

Supplemental Figure 3C **MACE Rate in both Rule-out groups**

ESC: European Society of Cardiology; Hs-cTnI: High-sensitivity cardiac troponin I; MACE: major adverse cardiac event; MACE+UA: major adverse cardiac event with unstable angina; UA: unstable angina; T1MI: Type 1 myocardial infarction; T2MI: Type myocardial infarction


A
MACE
≥ 62 years Troponin Alg.
≥ 62 years Extended Alg.
< 62 years Troponin Alg.
< 62 years Extended Alg.
p=0.297
p=0.792
p=0.478
p=0.594
MACE+UA
≥ 62 years Troponin Alg.
≥ 62 years Extended Alg.
< 62 years Troponin Alg.
< 62 years Extended Alg.
p<0.001
p<0.001
p<0.001
p<0.001
65 70 75 80 85 90 95 100
Sensitivity (%)
70 75 80 85 90 95 100
NPV (%)
B
MACE
Females Troponin Alg.
Females Extended Alg.
Males Troponin Alg.
Males Extended Alg.
p=0.141
p=0.330
p=0.654
p=0.918
MACE+UA
Females Troponin Alg.
Females Extended Alg.
Males Troponin Alg.
Males Extended Alg.
p<0.001
p=0.002
p<0.001
p=0.002
65 70 75 80 85 90 95 100
Sensitivity (%)
70 75 80 85 90 95 100
NPV (%)
C
MACE
CAD Troponin Alg.
CAD Extended Alg.
non-CAD Troponin Alg.
non-CAD Extended Alg.
p=0.681
p=0.932
p=0.223
p=0.396
MACE+UA
CAD Troponin Alg.
CAD Extended Alg.
non-CAD Troponin Alg.
non-CAD Extended Alg.
p<0.001
p=0.009
p=0.003
p=0.042
65 70 75 80 85 90 95 100
Sensitivity (%)
70 75 80 85 90 95 100
NPV (%)
D
MACE
CPO ≤2h Troponin Alg.
CPO ≤2h Extended Alg.
CPO >2h Troponin Alg.
CPO >2h Extended Alg.
p=0.680
p=0.955
p=0.340
p=0.636
MACE+UA
CPO ≤2h Troponin Alg.
CPO ≤2h Extended Alg.
CPO >2h Troponin Alg.
CPO >2h Extended Alg.
p<0.001
p=0.028
p<0.001
p=0.002
70 75 80 85 90 95 100
Sensitivity (%)
70 75 80 85 90 95 100
NPV (%)
E
MACE
eGFR ≤60 Troponin Alg.
eGFR ≤60 Extended Alg.
eGFR >60 Troponin Alg.
eGFR >60 Extended Alg.
p=1.000
p=0.658
p=0.093
p=0.250
MACE+UA
eGFR ≤60 Troponin Alg.
eGFR ≤60 Extended Alg.
eGFR >60 Troponin Alg.
eGFR >60 Extended Alg.
p=0.073
p=0.397
p<0.001
p<0.001
70 75 80 85 90 95 100
Sensitivity (%)
70 75 80 85 90 95 100
NPV (%)

Supplemental Figure 4	**Forest plots for sensitivity and negative predictive value including interaction p-value for the predefined subgroup analyses**

Forest plots indicating sensitivity and negative predictive values (NPV) for subgroup analyses (A: age, B: gender, C: known CAD, D: CPO, E: eGFR) in both the troponin and the extended algorithm including interaction p-values.

MACE: major adverse cardiac events; MACE+UA: major adverse cardiac event with unstable angina; CAD = coronary artery disease; CPO = chest pain onset; eGFR = estimated glomerular filtration rate